

6. ZARBL H, SUKUMAR S, ARTHUR AV, et al. Direct mutagenesis of Ha-ras-1 oncogenes by *N*-nitro-*N*-methylurea during initiation of mammary carcinogenesis in rats. *Nature* 1985;315:382-386.
7. QUINTANILLA M, BROWN K, RAMSDEN M, et al. Carcinogen-specific mutation and amplification of Ha-ras during mouse skin carcinogenesis. *Nature* 1986;322:78-80.
8. FUJITA J, YOSHIDA O, YUASA Y, et al. Ha-ras oncogenes are activated by somatic alterations in human urinary tract tumours. *Nature* 1984;309:464-466.
9. FUJITA J, SRIVASTAVA SK, KRAUS MH, et al. Frequency of molecular alterations affecting ras protooncogenes in human urinary tract tumors. *Proc Natl Acad Sci USA* 1985;82:3849-3853.
10. ITO N, ARAI M, SUGIHARA S, et al. Experimental urinary bladder tumors induced by *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine. *Gann Monogr Cancer Res* 1975;17:367-381.
11. CHANG EH, FURTH ME, SCOLNICK EM, et al. Tumorigenic transformation of mammalian cells induced by a normal human gene homologous to the oncogene of Harvey murine sarcoma virus. *Nature* 1982;297:479-483.
12. THOR A, HORAN HAND P, WUNDERLICH D, et al. Monoclonal antibodies define differential ras gene expression in malignant and benign colonic diseases. *Nature* 1984;311:562-565.
13. FURTH ME, DAVIS LJ, FLEURDELYS B, et al. Monoclonal antibodies to the p21 products of the transforming gene of Harvey murine sarcoma virus and of the cellular ras gene family. *J Virol* 1982;43:294-304.
14. SRIVASTAVA SK, YUASA Y, REYNOLDS SH, et al. Effects of two major activating lesions on the structure and conformation of human ras oncogene products. *Proc Natl Acad Sci USA* 1985;82:38-42.
15. REYNOLDS SH, STOWERS SJ, MARONPOT RR, et al. Detection and identification of activated oncogenes in spontaneously occurring benign and malignant hepatocellular tumors of the B6C3F1 mouse. *Proc Natl Acad Sci USA* 1986;83:33-37.
16. PAPAGEORGE A, DEFEO-JONES D, ROBINSON P, et al. *Saccharomyces cerevisiae* synthesizes proteins related to the p21 gene product of ras genes found in mammals. *Mol Cell Biol* 1984;4:23-29.
17. OHUCHI N, THOR A, PAGE DL, et al. Expression of the 21,000 molecular weight ras protein in a spectrum of benign and malignant human mammary tissues. *Cancer Res* 1986;46:2511-2519.
18. FUJITA J, NAKAYAMA H, ONONE H, et al. Frequency of active ras oncogenes in human bladder cancers associated with schistosomiasis. *Jpn J Cancer Res (Gann)* 1987;78:915-920.
19. HICKS RM. Nitrosamines as possible etiological agents in bilharzial bladder cancer. In: Magee PN, ed. Nitrosamines and human cancer. New York: Cold Spring Harbor Laboratory, 1982:455-471.
20. GALLICK GE, KURZROCK R, KLOETZER WS, et al. Expression of p21 ras in fresh primary and metastatic human colorectal tumors. *Proc Natl Acad Sci USA* 1985;82:1795-1799.
21. VIOLA MV, FROMOWITZ F, ORAREZ S, et al. Ras oncogene p21 expression is increased in premalignant lesions and high grade bladder carcinoma. *J Exp Med* 1985;161:1213-1218.
22. BROWN K, QUINTANILLA M, RAMSDEN M, et al. v-ras genes from Harvey and BALB murine sarcoma viruses can act as initiators of two-stage mouse skin carcinogenesis. *Cell* 1986;46:447-456.

Projections of Lung Cancer Mortality in the United States: 1985-2025¹

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Lung cancer has been the leading cause of cancer death in the United States for the larger part of this century. Increases in smoking prevalence from the 1900s through the 1950s have resulted in more than 100,000 deaths annually. Because of the changes during the last three decades in smoking prevalence, the decreasing tar content of cigarettes, and the increasing popularity of low-tar cigarettes, trends in lung cancer are difficult to predict. This article presents an analysis of smoking and lung cancer data using an age-period-cohort model for projecting lung cancer mortality through the year 2025. The projections are based on the initial parameterization of the model and on prevention objectives related to smoking behavior established by the National Cancer Institute. It is concluded that the recent trends in lung cancer are unlikely to be affected by changes in cigarette composition and consumption in the near term, but increasing the effectiveness of anti-smoking campaigns can have a considerable effect on lung cancer rates in the more distant future. [*J Natl Cancer Inst* 1988; 80:43-51]

Trends in lung cancer mortality during this century have been among the most remarkable phenomena in health statistics. From a relatively rare killer of both men and women in the early 1900s, lung cancer has developed into one of the biggest public health tragedies of the century, now claiming over 100,000 lives each year (1). Cancers of the lung and bronchus have been the most frequent cause of cancer death

ABBREVIATIONS USED: HIS = Health Interview Survey; ICD = International Classification of Diseases; NCI = National Cancer Institute.

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of males in the United States for the past 40 years and were the second most frequent cause of cancer death among U.S. females for the past two decades. Recently, lung cancer has nearly surpassed breast cancer in age-adjusted mortality rates for women (2).

Because lung cancer is such a major contributor to the overall U.S. cancer mortality picture, its reduction is of the greatest priority among all the various groups involved in cancer control. However, the implementation of effective cancer control strategies and their evaluation will depend to some degree on what is likely to happen to lung cancer trends in the absence of any new major cancer control activities. The purpose of this article is to present projections of lung cancer mortality rates through the remainder of this century and the first three decades of the next. These projections are of considerable interest to the public health community not only because they will suggest the coming mortality for one of the major causes of death, but also because they reflect the general health burden for a variety of diseases related to smoking.

Although studies showing that cigarette smoking is the major determinant of lung cancer were presented to the scientific community as early as 1950, it was not until the first Surgeon General's report on smoking and cancer in 1964 that this relationship was established in a widely accepted public forum (3). Therefore, it is not surprising in reviewing the evidence concerning cigarette smoking patterns in the United States that the decades between the end of the First World War and the Surgeon General's report were marked by a substantial increase in the per capita consumption of cigarettes, with a particularly rapid growth during the Second World War (4). Because there is a considerable lag time between beginning smoking and the development of cancer [e.g., Doll and Peto (5)], the effects of the tremendous increase in smoking have been seen in the lung cancer mortality statistics in the decade of the 1970s.

Two phenomena of recent decades may have led to the beginning of changes in the lung cancer picture for the 1980s and beyond (4). Recent data have shown considerable declines in the smoking prevalence among U.S. males, but slower declines for U.S. females (6,7). These declines among men began with the release of the 1964 Surgeon General's report and continued with the removal of cigarette advertising from television. Reduction in tar content of all brands of cigarettes and the introduction of low-tar brands beginning in the late 1960s should also lead to lower lung cancer risks even without prevalence changes.

Changes in the prevalence of smoking and tar content of cigarettes have already affected U.S. incidence and mortality rates for men under age 55 (8,9). However, no such decline is yet seen in women, which no doubt reflects their dramatic increases in smoking prevalence during the 1960s and 1970s.

These complex changes in smoking behavior over time have lead to morbidity and mortality patterns that have engendered much research (10-16). These articles have generally attempted to explain the distinct patterns in lung cancer mortality by various models, sometimes taking ex-

plicit account of smoking trends. Despite the use of a variety of models fitting available mortality data, there has been little published to date on projections of those trends. One such projection by Janerich (17) using a simple model suggests that lung cancer mortality will continue to rise at a rapid rate and will dominate mortality trends for the near future. Fortunately, this rapid increase is not likely to be realized, as recent reports (8) continue to show the decline in lung cancer incidence among U.S. males. Clearly, a sophisticated modeling approach to these trends is needed and, preferably, one that takes into account available data on past smoking behavior.

Subjects and Methods

The analyses presented in this article are based on the numbers of deaths from malignant neoplasms of the trachea, bronchus, and lung (ICD 162-163.0, eighth revision) occurring among white males and females in the United States during 1958-1982. We have not used data prior to 1958 because the ICD coding changed at this time. The data, numbers of deaths and person-years at risk, have been aggregated into 12 age groups (30-34, 35-39, . . . , 80-84, ≥ 85) and 5 calendar year periods (1958-1962, . . . , 1978-1982). Person-years at risk are approximated by mid-year population estimates.

Our estimates of past smoking prevalence are derived from cigarette smoking histories from the 1978-1980 HIS conducted by the U.S. National Center for Health Statistics. Details of the HIS, a stratified, household-based, personal interview survey, are reported elsewhere (18). The respondents in this survey numbered 22,990 males and 26,725 females age 17 or older at the time of the interview. Less than 1% of the interviews were proxies and were not included in our analysis. For each individual, a history of smoking status was derived from answers to the questions of current smoking status, age started smoking regularly, and the time since last smoked regularly. Those who never smoked cigarettes regularly were classified as nonsmokers for their life. Former smokers were classified as nonsmoking from the age they reported cessation of regular smoking. Those reported as ever smoking with partially missing information were classified according to the following assumptions: 1) When the age at initiation of regular smoking was unknown ($<0.5\%$), the modal age of 18 was used; 2) when a self-reported former smoker's time since cessation was unknown (1.6%), the time was assumed to be zero; 3) individuals who were coded as having unknown current smoking status but did report an age of initiation (0.2%) were treated as current smokers.

Because cigarette smokers have higher mortality rates than nonsmokers, estimates of past cigarette smoking prevalence based on currently living persons will understate the actual prevalence. We therefore followed the approach of Harris (6) to correct for this bias. Using his notation, we let P_u and Q_u denote the proportions of current and former smokers at age t among respondents alive at age $u > t$. An

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estimate of the prevalence of cigarette smoking at age t , $u - t$ years in the past, is given by

$$P_{it}(u) = \frac{P_{iu}/S_{iu}}{P_{iu}/S_{iu} + Q_{iu}/F_{iu} + (1 - P_{iu} - Q_{iu})/N_{iu}} \quad [1]$$

where S_{iu} , F_{iu} , and N_{iu} represent the probabilities of surviving from age t to age u for current smokers, former smokers, and never smokers, respectively. Estimates of S_{iu} and N_{iu} are from the American Cancer Society study (Garfinkel L: personal communication). We did not have estimates of F_{iu} , so, assuming former smokers would experience mortality more similar to that of smokers than never-smokers, we used S_{iu} to represent their survival.

The 3 survey years provided three estimates of the age-specific smoking prevalence for each year in the past. These were combined into a single estimate weighted by the number of persons interviewed. For example, individuals aged 70 and interviewed in 1978, those aged 71 and interviewed in 1979, and those aged 72 and interviewed in 1980 contributed to the estimate of the proportion of smokers aged 42 in 1950.

Because the trends over time in lung cancer morbidity and mortality are strongly related to changes in cigarette smoking and the composition of cigarettes (4,19,20) and because the latent period for lung cancer occurrence may be 20–40 years, past changes in smoking behavior and cigarette composition should be an important aspect of any projection of future lung cancer rates. The prevalence of cigarette smoking has been changing from one birth cohort to the next (6), and the introduction of low-tar cigarettes has greatly reduced the average tar content of cigarettes sold in the United States (fig. 1). Whereas changes in smoking prevalence should produce birth cohort effects in the trends of lung cancer mortality, changes in cigarette composition affecting smokers across different birth cohorts at the same calendar time should produce calendar period effects in the lung cancer mortality trend.

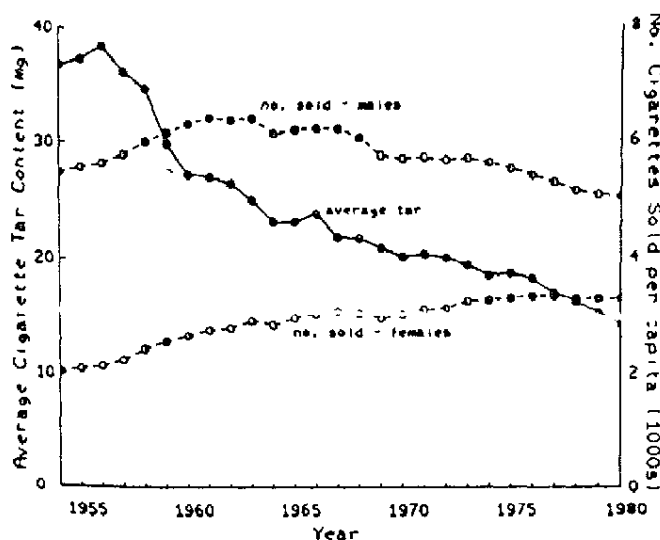


Figure 1. Average tar content of cigarettes sold and age-adjusted smoking prevalence of adults in the United States, 1954–1980.

For these reasons we have based our statistical analysis of lung cancer mortality on an age-period-cohort model (21,22). This type of statistical model has been used previously for cohort analyses of lung cancer (23,24) but has not been used to project future disease occurrence. This model assumes that the number of cancer deaths D_{ij} observed in age group i during calendar period j follows a Poisson probability distribution with mean $\mu_{ij} = N_{ij}r_{ij}$, where N_{ij} denotes the size of the population at risk and r_{ij} denotes the rate of cancer mortality. The r_{ij} are modeled as a function of age, calendar period, and birth cohort. More specifically, it is assumed that

$$\log(r_{ij}) = A_i + P_j + C_{I-i+j}, \text{ for } i = 1, 2, \dots, I \text{ and } j = 1, 2, \dots, J, \quad [2]$$

where A_i ($i = 1, 2, \dots, 12$) denotes the age effect for ages 30–34, 35–39, ..., 80–84, ≥ 85 ; P_j ($j = 1, 2, \dots, 5$) denotes the period effect for calendar periods 1958–1962, 1963–1967, ..., 1978–1982; and C_k ($k = 1, 2, \dots, 16$) denotes the cohort effects for birth cohorts 1869–1877, 1874–1882, ..., 1944–1952.

The model is then fit to the data by maximum likelihood methods. A linear dependency ($k = I - i + j$) exists among the three factors age, calendar period, and birth cohort, which induces a nonidentifiability of the linear components of the three sets of parameter estimates (25–27). This nonidentifiability means that we cannot estimate the linear component of trends over time for the period and cohort effect parameters. Therefore, we cannot determine whether the period effect parameters are increasing while the cohort effect parameters are decreasing or vice versa. The nonlinear components of each factor, however, are estimable (26). Unfortunately, the increasing or decreasing linear trends of the individual period and cohort factors are often of primary interest.

A number of solutions have been proposed for this nonidentifiability problem. Most of these involve constraints to be placed on the parameters; however, the parameter estimates have been shown to be sensitive to the choice of constraint (27). The change in parameter estimates from use of one constraint to another can be so extreme as to preclude meaningful interpretation. Therefore, unless there is a very compelling reason for choosing a particular constraint, this approach will not provide a satisfactory solution. Another method, proposed by Day and Charnay (23), requires two or more populations, one of which can be adequately fit by a two-factor model. We found this approach was not applicable because we could not satisfactorily describe either the male or female deaths by a two-factor model. Other proposed solutions involve finding the single three-factor model that is "closest" to the best fitting two-factor model (25,28). However, these approaches are ad-hoc statistical solutions that have no biological justification.

Rodgers (29) suggested that a valid solution could be obtained by replacing one of the factors with a more directly relevant variable for which the factor is thought to be an indirect indicator. This is the approach we have used here. As suggested by Day and Charnay (23) in their analysis of lung cancer in Slovenia and Finland, one would expect the trend of changing cigarette tar content to be reflected in lung

cancer mortality as a calendar period effect acting across all age groups. Therefore, we followed Rodgers' approach by replacing the period parameters in equation 2 with a regression variable related to the average tar content and number of cigarettes sold. Thus our model is

$$\log(r_{ij}) = A_i + BX_j + C_{l-i+j}, \quad [3]$$

where the period parameter of equation 1 is replaced by a regression on X_j which denotes a measure of the population's exposure to cigarette tar during the j th calendar period.

Results

To fit the model in equation 3 to the observed lung cancer mortality data, we evaluated two exposure measures for the variable X_j : (1) the average tar content of cigarettes sold in the United States and (2) the product of average tar and the number of cigarettes sold per capita (age ≥ 20) as a measure of the entire population's average exposure level. Figure 1 shows the changing average tar content of cigarettes sold (30,31) along with estimates of the number of cigarettes sold per capita to males and females for the period 1954-1980. Our estimates of the sex-specific numbers of cigarettes sold are derived from age-adjusted smoking prevalence estimates applied to the total annual cigarette sales. Our smoking prevalence estimates are based on applying the estimator in equation 1 to the HIS data to derive age-specific prevalence rates aggregated into 5-year age groups. Table 1 shows that the age-specific prevalences of past smoking as estimated from the 1978-1980 HIS generally agree (an average difference of 3.6%) with prevalences estimated from actual surveys conducted in 1966, 1970, and 1975. We then used the 1970 standard U.S. population age distribution to obtain direct age-adjusted smoking prevalence rates back through 1954. Since the HIS data did not provide age-specific prevalence rate estimates for the age groups 80-84 and ≥ 85 during the earliest time periods, we used the rates based on our estimates for 1975. The error induced by this should have little impact, since few people were in these age groups.

Table 1. Estimated prevalence of current smokers according to age and sex in the United States, 1966-1975

Sex	Age (yr)	1966		1970		1975	
		Survey*	HIS†	Survey	HIS†	Survey	HIS†
Males	20-24	61.9	56.2	49.8	52.4	41.3	46.5
	25-34	59.9	56.2	46.7	52.6	43.9	50.4
	35-44	59.0	57.4	48.6	53.0	47.1	47.2
	45-54	53.8	54.3	43.1	51.1	41.1	47.3
	55-64	47.7	44.2	37.4	42.0	33.7	41.6
	≥ 65	27.8	25.9	22.8	28.1	24.2	27.9
Females	20-24	49.2	43.1	32.3	38.7	34.0	37.5
	25-34	45.1	43.2	40.3	43.0	35.4	39.8
	35-44	40.6	40.9	38.8	39.6	36.4	39.9
	45-54	42.0	36.5	36.1	36.9	32.8	36.4
	55-64	20.6	21.6	24.1	26.9	25.9	30.1
	≥ 65	7.6	8.0	10.2	11.4	10.2	15.1

*From (41); separate surveys were done in 1966, 1970, and 1975.

†Estimated from 1978-1980 HIS as described in text.

Figure 1 shows a steady decrease in the sales-weighted average cigarette tar content from 37.5 mg in the mid-1950s to 14 mg in 1980, a drop of over 60%. The estimated number of cigarettes sold to males peaked between 1960 and 1965 and has declined steadily since then, whereas the estimated number sold to females has risen over this period. When fitting the model in equation 3, we used 5-year averages of the average tar content or of the product of average tar and number sold. Because changes in carcinogenic exposure are not reflected immediately in changing cancer mortality, we examined possible lag periods between our exposure measures and mortality when fitting the regression model in equation 3. Information on the average tar content of cigarettes sold before 1954 is not available. Since filter cigarettes were originally introduced in the mid-1950s, one assumption is that tar content underwent little change before this time (Warner K; personal communication). Therefore, we assumed the pre-1954 average cigarette tar content to be the average of the 1954-1958 levels, 36.6 mg. On the basis of minimizing the deviance as a measure of goodness-of-fit, we concluded that the best exposure regressor variable is the product of average tar content and number of cigarettes sold, lagged for 24 years. Peace (32) found a 21-year lag when correlating overall lung cancer mortality with cigarette tobacco sales by weight in England and Wales during 1880-1983. However, his analysis was not adjusted for age and birth cohort.

In addition to changes in tar content of cigarettes, there have been other changes that probably have affected lung cancer patterns. Changes in air pollution and occupational exposure head the list. We judge these likely to be very small in comparison to cigarette smoking. The relative risk of occupational exposures that might serve as an upper bound for the effect of environmental carcinogens is on the order of 1.4-3.2 (33), and these apply to small proportions of the population, leaving a small attributable risk. Others have suggested a minor role for pollutants (4), and the evidence from time trends in nonsmokers does not substantiate any temporal effect in environmental carcinogens (34). Finally, recent evidence from a large case-control study in Western Europe shows substantial reductions in lung cancer incidence attributable to lower tar cigarettes (35-37).

To assess whether separate regression coefficients were needed for males and females and for different age groups, we compared the fit of various models using an analysis of deviance (38). Our analysis indicated that the slope of the average tar content \times number cigarettes sold exposure variable differs by both sex and age. A statistical test of equal slopes for males and females yields a one degree of freedom chi-square value of 37.6, while a test for equal slopes for under age 50 and ≥ 50 yields a value of 155, both highly significant ($P < .001$). We examined other age group categorizations and found the under/over 50 to give the best fit. As shown in tables 2 and 3, females have a larger slope than males and the under-50 group has a larger slope than the over-50 group. These differences are consistent with surveys beginning in the late 1960s that have shown that males and older persons are more likely to continue to smoke higher tar cigarettes (39). Therefore, decreases in tar levels would be

expected to have a greater effect on lung cancer among females and younger persons. Thus our final model that we fit to male and female lung cancer mortality is

$$\log(r_{ij}) = \begin{cases} A_i + B_1 X_j + C_{I-i+j} & i \leq 4 \\ A_i + B_2 X_j + C_{I-i+j} & i \geq 5 \end{cases} \quad [4]$$

where B_1 is the regression coefficient for ages 30-49 and B_2 is the coefficient for ages ≥ 50 .

Parameter estimates of the age, period, and birth cohort effects for males and females are given in tables 2 and 3,

Table 2. Parameter estimates from fitting model in equation 4 to male lung cancer mortality

Age (yr)		Birth cohort	
30-34	-12.92	1869-1877	0.13
35-39	-11.77	1874-1882	0.37
40-44	-10.79	1879-1887	0.64
45-49	-9.95	1884-1892	0.96
50-54	-9.01	1889-1897	1.22
55-59	-8.43	1894-1902	1.42
60-64	-7.91	1899-1907	1.56
65-69	-7.54	1904-1912	1.64
70-74	-7.25	1909-1917	1.72
75-79	-7.08	1914-1922	1.79
80-84	-6.98	1919-1927	1.85
≥ 85	-7.01	1924-1932	1.92
Slope of average tar \times No. sold		1929-1937	1.87
		1934-1942	1.75
Age 30-49 yr	2.24×10^{-3}	1939-1947	1.52
Age ≥ 50 yr	0.92×10^{-3}	1944-1952	1.21

Table 3. Parameter estimates from fitting model in equation 4 to female lung cancer mortality

Age (yr)		Birth cohort	
30-34	-13.42	1869-1877	-1.20
35-39	-12.20	1874-1882	-1.04
40-44	-11.19	1879-1887	-0.92
45-49	-10.36	1884-1892	-0.77
50-54	-9.55	1889-1897	-0.59
55-59	-8.95	1894-1902	-0.33
60-64	-8.40	1899-1907	-0.01
65-69	-7.93	1904-1912	0.36
70-74	-7.52	1909-1917	0.75
75-79	-7.21	1914-1922	1.07
80-84	-6.96	1919-1927	1.29
≥ 85	-6.77	1924-1932	1.50
Slope of average tar \times No. sold		1929-1937	1.60
		1934-1942	1.58
Age 30-49 yr	5.38×10^{-3}	1939-1947	1.49
Age ≥ 50 yr	3.28×10^{-3}	1944-1952	1.29

respectively. The male lung cancer mortality rate peaks for the cohort born around 1928, while the rate for females attains a peak for the cohort born around 1933. Since the age and cohort parameters are unique up to an additive constant, we adjusted the age parameters to reflect the age-adjusted mortality rates among nonsmokers (34). This was done so the model would predict what the effect of eliminating smoking would be to attain nonsmoker mortality rates.

Day and Charnay (23) suggested interpreting the cohort parameters as reflecting the number and type of cigarettes a

cohort becomes habituated to smoking when young. To examine this interpretation, figures 2 and 3 compare the time patterns of the sex-specific cohort parameter estimates with the age-specific cigarette smoking prevalence estimates among males aged 20-24 and females aged 30-34 for different birth cohorts. Because the prevalence of smoking for a cohort peaks around these ages, this age-specific prevalence is hypothesized to represent a measure of smoking habits by birth cohort, which becomes translated into the cohort parameters in our mortality model. The age at which this prevalence reaches a peak has changed over the years. For cohorts born around 1900, the peak prevalence was reached around age 30 for men and age 45 for women. More recent cohorts have shown a peak at 20-24 for males and 25-29 for females.

Both figures show that each set of estimated cohort parameters for lung cancer mortality exhibits a pattern quite similar to that of our cohort smoking behavior index. The time patterns of the cohort parameters and cohort smoking index exhibited by the females are very similar to one another (correlation coefficient of 0.99), while the pattern of the male cohort smoking index appears less regular than the female pattern (correlation of 0.83). We hypothesize that the male pattern has been affected by the Depression, reducing the smoking index for cohorts born from 1905 to 1920. These figures indicate that our proposed cohort smoking index provides a good representation of the cohort parameters in our age-period-cohort model, and this correlation will be used for the projections in the following section.

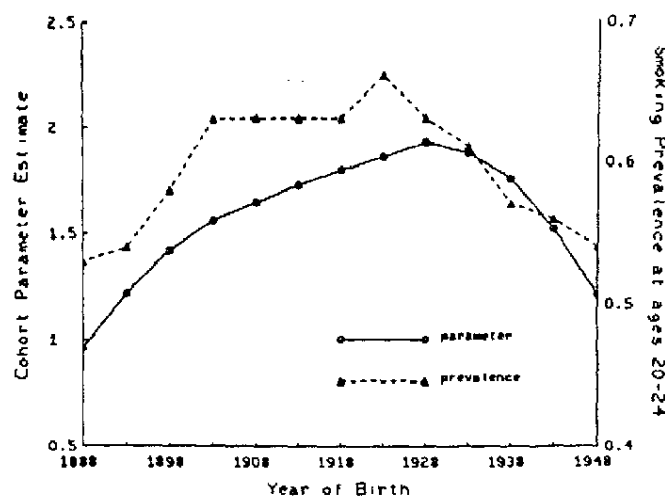


Figure 2. Comparison of estimated cohort parameters and prevalence of smoking at ages 20-24 for U.S. white males.

Basis for projections. To make projections of lung cancer mortality, our age-period-cohort model requires projections of the parameters of the period and cohort factors. Our assumption that the age parameters remain fixed at their estimated values is consistent with our interpretation that they represent the background level of lung cancer risk in a nonsmoking population. Because lung cancer risk is primarily the result of cigarette smoking, our estimates of the future period and cohort factors are based on projections of future

cigarette composition and consumption. From the model in equation 4, the period parameters are linear functions of the product of average cigarette tar content with the number of cigarettes sold, while figures 2 and 3 show that the cohort parameters can be estimated as functions of the prevalence of smoking among young adults. Therefore, we need to project: (1) the average tar content of cigarettes sold in the United States, (2) the number of cigarettes sold in the United States, and (3) the prevalence of smoking among young adults.

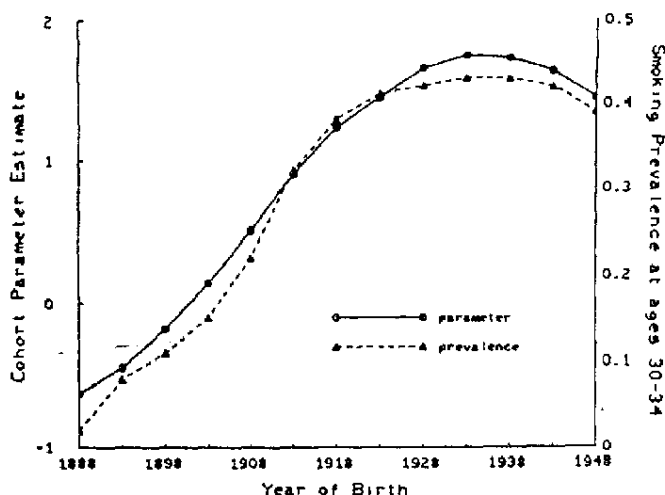


Figure 3. Comparison of estimated cohort parameters and prevalence of smoking at ages 30-34 for U.S. white females.

Projecting tar content in the future is somewhat difficult because the sales-weighted averages shown in figure 1 are a combination of changes in the production of virtually all cigarettes made in the United States, the development of filters and of new low-tar brands in the last three decades, and changes over time in the proportion smoking various types. In addition, the trends in these data are quite strong and almost linear; however, a linear decrease cannot continue unabated, and the point at which one might choose to "level off" these projections is speculative. Surveys have shown that smokers of high-tar (especially unfiltered) cigarettes are generally concentrated among the elderly (19), and these individuals will soon die off, creating further declines in the sales-weighted average tar level. In addition, as the proportion of women in the smoking population increases, the market share of high-tar cigarettes will likely further decrease.

For the projections to follow, we assume sales-weighted tar will continue to decrease in a linear fashion until reaching the optimistic level of 5 mg per cigarette and then level off. This linear trend is estimated from the 1972-1981 average tar content values, when the estimated yearly decrease was 0.74 mg. In a second scenario we took the conservative view of leaving the sales-weighted tar constant at 13.22 mg per cigarette, the 1981 value.

A projection of the future number of cigarettes sold in the United States requires projections of future smoking preva-

lence among all adults and the average number of cigarettes purchased by each smoker. Developing projections for smoking prevalence, we relied on the objectives developed by the NCI for the Year 2000 Project (40). The NCI has set a goal of decreasing the smoking prevalence from current levels to 15% of all adults by the year 1990. Our smoking prevalence projections are based on assuming a linear decrease in the age-adjusted (ages ≥ 15 adjusted to the 1980 population) smoking prevalence from the levels of 40.6% for males and 32.3% for females estimated from the 1978/1980 HIS. To project our exposure index of the tar \times number sold per capita, we assume that the average number of cigarettes sold per smoker would remain at the 1980 levels. Therefore, the projected values of our tar \times number sold index is the product of the projected tar level, the projected prevalence of smoking, and the number of cigarettes sold to smokers. These projections, along with the values observed in the past, are given in table 4.

Because of our estimated 24-year lag, these average levels during 1934/1938, . . . , 1954/1958 provide the calendar period component of the fitted mortality rates for the periods 1958/1962, . . . , 1978/1982, while the actual and projected levels for the years 1959/1963 through 1999/2003 are components of our mortality rate projections through the period 2023/2027.

As seen in figures 2 and 3, the pattern of fitted cohort parameters in our mortality model is similar to the pattern of smoking prevalence among young adults. Therefore, we use projections of the age-specific prevalence of smoking for males aged 20-24 and females aged 30-34 to estimate future cohort parameters for our mortality projections. We

Table 4. Actual and projected 5-year averages of tar \times number of cigarettes sold (in 1,000s) per capita

Years	Averages	
	Males	Females
<i>Actual</i>		
1934/1938	108.9	22.1
1939/1943	145.3	36.0
1944/1948	203.1	58.9
1949/1953	212.8	72.7
1954/1958	207.6	79.6
1959/1963	169.2	72.7
1964/1968	137.9	66.4
1969/1973	113.6	61.2
1974/1978	94.8	57.7
<i>Projected*</i>		
1979/1983	59.4	48.1
1984/1988	35.3	31.4
1989/1993	18.0	17.9
1994/1998	14.1	14.1
1999/2003	14.1	14.1

*We assume: (1) tar content to decrease linearly to 5 mg in 1993 and (2) smoking prevalence to decrease linearly to 15% for all adults in 1990.

found that the best fitting functional relationship between young adult smoking prevalence and the cohort parameters to be $Y_i = bX_i^2$, where Y_i represents the fitted cohort parameter and X_i represents the smoking prevalence for the i th birth cohort ranging from 1888 to 1948. This relationship assumes no intercept so that as the smoking prevalence

decreases to zero the cohort parameters would also go to zero and the age-specific lung cancer mortality risk would become the 1958-1968 nonsmokers' risk as noted in the previous section. The regression for males was estimated by least squares applied to the data in figure 2, which resulted in an estimated slope $\hat{b} = 4.4$. The regression for females was estimated from the 1908-1948 data shown in figure 3 and resulted in an estimated slope of $\hat{b} = 8.2$.

Following the Year 2000 Project objectives, one scenario is that the prevalence of smoking among young adults drops to 15% by the year 2000. Our smoking prevalence projections for males aged 20-24 assume a linear decrease from the 41% observed for those born during 1956-1960 to 15 or 0% for those born during 1976-1980 (being 20-24 in the year 2000). The projections for females aged 30-34 decrease linearly from the observed 39% for those born during 1946-1950. The smoking prevalence projections assuming 15% prevalence by the year 2000 are given in table 5.

Table 5. Projection of smoking prevalence among young adults*

Year of birth	Smoking prevalence†	
	Males	Females
1946-1950	(0.54)	(0.39)
1951-1955	(0.48)	0.33
1956-1960	(0.41)	0.27
1961-1965	0.345	0.21
1966-1970	0.28	0.15
1971-1975	0.215	0.15
1976-1980	0.15	0.15

*Cell entries are smoking prevalence for males of ages 20-24 and females of ages 30-34 by birth cohort; both sexes assumed to have 15% prevalence of smoking by the year 2000 in their respective age groups; as explained in the text, cohort parameters are given by:

$$\begin{aligned} \text{Males: } \text{parameter} &= 4.4 \times (\text{smoking prevalence})^2 \\ \text{Females: } \text{parameter} &= 8.2 \times (\text{smoking prevalence})^2 \end{aligned}$$

†Observed prevalence in parentheses.

Projections of mortality. The age-adjusted projections are shown in table 6 and figure 4 for the NCI objectives compared to a "baseline" alternative in which tar content and smoking prevalence are assumed not to change after 1980. For both males and females, but especially for males, the two sets of projected rates for the period 1998/2002 differ very little because of the estimated 24-year lag for the effect of changes in tar content and age-adjusted smoking prevalence. The only changes in our mortality projections in this short time span are due to different cohort effects, and these will affect only the young age groups with low mortality rates before the end of this century. For males, the projected year 2000 age-adjusted rate under the NCI objectives is 68.1 per 100,000, just 0.7% less than the rate of 68.6 per 100,000 for the no-change scenario. The differences in mortality rates projected for the period 2023/2027 between the two scenarios are noticeably larger. The projected rates for males are 43.0 and 28.8 per 100,000 for the no-change and NCI scenarios, respectively, representing a 33% decline due to accomplishing the NCI's smoking objectives. A larger difference is apparent for females for the 2023/2027 period;

Table 6. Actual and projected age-adjusted lung cancer mortality rates per 10⁵

Years	Actual rates			
	Males		Females	
1958/1962	38.1		5.8	
1963/1967	47.3		7.5	
1968/1972	57.9		11.1	
1973/1977	65.2		15.2	
1978/1982	71.0		20.6	
	Projected rates			
	Males		Females	
	NCI obj.*	No change	NCI obj.*	No change
1983/1987	72.6	72.6	25.6	25.6
1988/1992	72.9	73.0	30.8	30.8
1993/1997	71.5	71.7	35.4	35.6
1998/2002	68.1	68.6	38.9	39.5
2003/2007	61.3	64.6	39.6	42.3
2008/2012	52.8	58.9	36.2	43.2
2013/2017	44.5	52.7	32.9	42.6
2018/2022	36.1	47.0	28.3	40.8
2023/2027	28.8	43.0	23.4	38.8

*NCI objectives: (1) tar content decreases linearly to 5% in 1993, (2) age-adjusted smoking prevalence drops to 15% in 1990, and (3) smoking prevalence in young adults drops to 15% in 2000.

there is a 40% difference in the projected rates, from 38.8 to 23.4 deaths per 100,000.

Varying each of the three elements of the projection model, tar, age-adjusted smoking prevalence, and age-specific prevalence among new smoking cohorts, produces different projection tables for males and females. We examined more conservative projections, for example, tar levels not decreasing below 1982 levels and age-adjusted prevalence not declining below 25% for adults, as well as more liberal projections, including, for example, no new smokers among young adults by the year 2000. For the near term, the period 1998/2002, the differences in age-adjusted

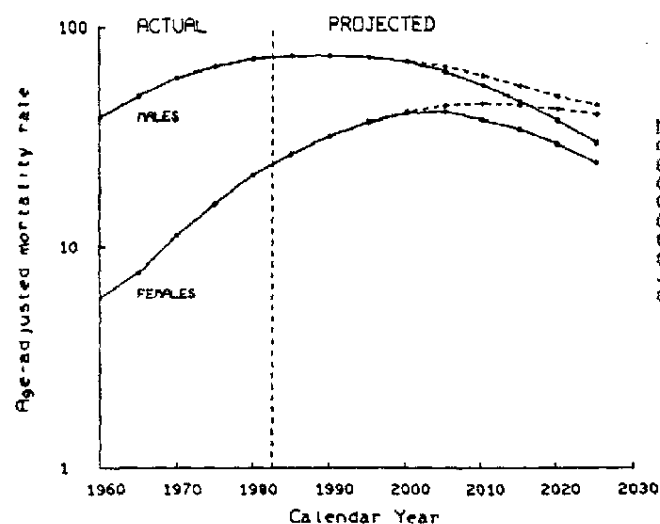


Figure 4. Actual and projected age-adjusted lung cancer mortality rates for U.S. white males and females, 1960-2025. — = NCI objectives; --- = no change.

rates are trivial. As the projection horizon lengthens, the differences become more noticeable. However, the rates based on more liberal objectives are similar to the NCI objective projections, illustrating that accomplishment of the NCI objectives (tar declines linearly, smoking prevalence at 15%) would include much of the potential reduction in lung cancer mortality for the next several decades. We considered the more dramatic scenario of a 0% prevalence of smoking by the year 2000 and obtained similar results. For example, under this scenario, the projected male age-adjusted mortality rate for the period 2023/2027 is 27.9 per 100,000, only 3.1% less than the projection of 28.8 based on the NCI objectives. Females show a larger relative decline of 11% from 23.4 deaths per 100,000 to 20.9 in the 2023/2027 period. These detailed age-specific projection tables are available from the authors upon request.

Projections at the age-specific level better illustrate why the rate of decline in the age-adjusted projections is so slight. When the different effects begin to be seen in each of the age groups and how fast these rates drop are crucial to interpreting the plausibility of the projections. As shown for males in figure 5, by the year 2000 only the age groups under 45 are affected by the decrease in new smokers represented by attaining the NCI objectives. For groups older than age 45, changes are not apparent until later. For males aged 55-59, the recent (1978/1982) lung cancer mortality rates are 169 per 100,000. Under the no-future-change model, these are projected to be 109 in the year 2000 and lower still to 80.5 by the year 2025. Therefore, the no-change scenario includes a substantial decline in lung cancer mortality for this younger age group to begin in the near future and to carry through this projection horizon due to changes in tar content and smoking prevalence that have already occurred. Achievement of the NCI objectives would further reduce these rates to 31.2 in 2025. A similar picture is evident for older males. Among the 75-79 year olds, compared to a recent rate of 487, the no-change scenario projects rates of 587 for the year 2000 and 311 by the end year of the projections (2025). The decline in mortality rates for this age group begins about the year 2005, 20 years after the turnaround for the 55-59 year age group. The general age-specific pattern for females is quite similar, but shows a later period of peak mortality rates (fig. 6). For the 55-59 year age group, the peak mortality rate of 79.6 is projected to be in the 1988/1992 period, 5 years later than males. The female rates for this age group for the years 2000 and 2025 are projected to be 69.4 and 56.9, respectively, under the no-change scenario. Attaining the NCI objectives reduces the later projected rates to 13.0 per 100,000.

Discussion

Trends in the United States during the past two decades have shown a dramatic turnaround in smoking prevalence. Because of these trends, changes in lung cancer and other tobacco-related diseases have been eagerly anticipated. Declines in age-specific rates of lung cancer for young ages have been seen recently as a result of lower smoking prevalence among new cohorts and as a result of lower tar content

in cigarettes. However, age-adjusted rates of lung cancer mortality have continued to climb for males, although recently there has been a noticeable flattening of these rates. For U.S. females, however, incidence and mortality rates have continued to dramatically increase.

In the present analysis, we have constructed a model to take account of these trends of major public health interest and have provided a framework for projecting rates into the future. The model is based on age-period-cohort modeling, which has been used extensively in cancer epidemiology. In addition to fitting the model to available lung cancer mortality data, we have analyzed recent survey data on cigarette consumption and incorporated these findings into the projection model. This allows the projection of lung cancer rates, providing one is willing to make a set of assumptions about the three key factors that we believe are the major determi-

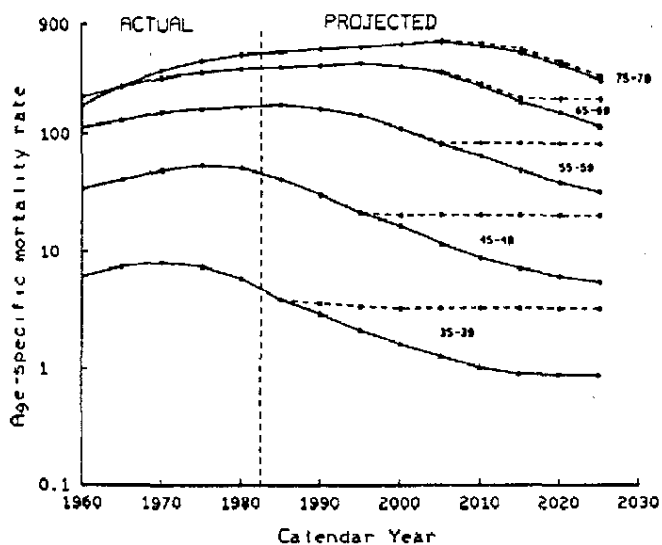


Figure 5. Actual and projected age-specific lung cancer mortality rates for U.S. white males, 1960-2025. — = NCI objectives; --- = no change.

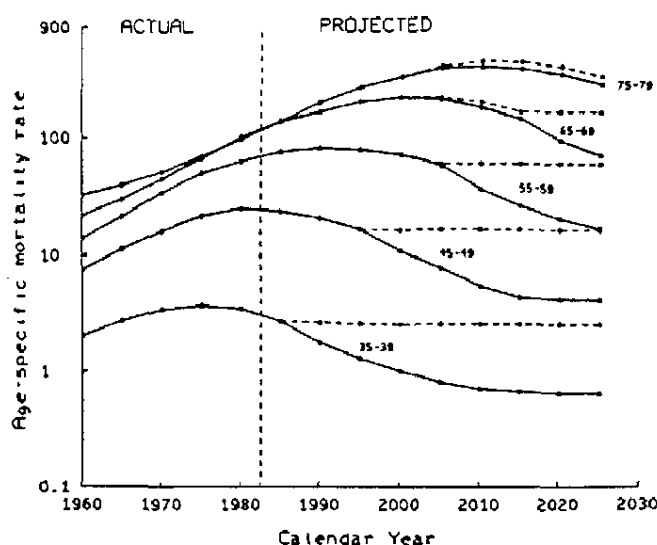


Figure 6. Actual and projected age-specific lung cancer mortality rates for U.S. white females, 1960-2025. — = NCI objective; --- = no change.

nants of lung cancer mortality: starting the smoking habit, continued smoking prevalence, and tar content of cigarettes.

Projections of lung cancer rates in the absence of any major changes in these factors show that the age-adjusted rates in males will be relatively flat through about 1990 and will then gradually decline. Mortality patterns for females lag behind those for males, and in the absence of changes, rates are projected to peak about the year 2010. The age-specific peaking for females is only 5 years behind that for males; the age-adjusted rates peak later for females because of their more recent increase in smoking prevalence.

Achievement of objectives for reducing smoking prevalence advocated by the NCI will have little impact on these trends in the very near future. Little material changes can be expected by the year 2000 based on the empirical findings here; however, the longer term impact of the NCI objectives is much more positive. Compared to no changes in smoking prevalence and cigarette tar content, attaining the NCI objectives could reduce the age-adjusted male lung cancer mortality rate by almost 33% by the period 2023/2027 and the female mortality rate could be reduced by over 40%. Assuming attainment of the NCI objectives, we note that the projected age-adjusted rate for males for the period 2023/2027 of 28.8 per 100,000 represents almost a two-thirds reduction of the 1978/1982 mortality rates. Although the rate of 23.4 per 100,000 for females in 2023/2027 is about equal to recent rates, this is a considerable reduction on what would be projected under current trends. Advances in secondary and tertiary prevention represented by screening and treatment might also affect future lung cancer mortality trends, but we have limited our analysis to the future effects of cigarette smoking behavior.

We are somewhat surprised by the intractability of the rates in the near future. However, the empirical fit of the model to the data suggested lagged effects for parameters, which are consistent with previous literature (32). Thus reduction in lung cancer mortality rates in the next decade or two will occur only if recent decreases in smoking prevalence continue and efforts to reduce smoking further are adopted throughout the United States.

References

- SILVERBERG E, LUBERA J. Cancer statistics, 1986. CA 1986;36:9-25.
- American Cancer Society. Cancer statistics, New York: Am Cancer Soc, 1985.
- US Public Health Service. Smoking and health. Report of the Advisory Committee to the Surgeon General of the Public Health Service, US Department of Health, Education, and Welfare. Washington, DC: US Govt Print Off, 1964 (PHS publication No. 1103).
- DOLL R, PETO R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. JNCI 1981;66:1191-1308.
- DOLL R, PETO R. Cigarette smoking and bronchial carcinoma: dose and time relationships among regular smokers and lifelong non-smokers. J Epidemiol Community Health 1978;32:303-313.
- HARRIS J. Cigarette smoking among successive birth cohorts of men and women in the United States during 1900-60. JNCI 1963;71:473-479.
- WILSON RW, AAVEDAL MJ. Smoking data from the National Center for Health Statistics. Presented at the American Public Health Association, November 1984.
- HORM JW, KESSLER LG. Falling rates of lung cancer in men in the United States. Lancet 1986;1:425-426.
- DEVESA SS, HORM JW, CONNELLY RR. Trends in lung cancer incidence and mortality in the United States. In: Mizell M, Correa P, eds. Lung cancer: causes and prevention. Deerfield Beach, FL: Verlag Chemie Int, 1984;33-45.
- SCHNEIDERMAN MA, LEVIN DL. Trends in lung cancer: mortality, incidence, diagnosis, treatment, smoking, and urbanization. Cancer 1972;30:1320-1325.
- BURBANK F. U.S. lung cancer death rates begin to rise proportionately more rapidly for females than for males: a dose-response effect? J Chronic Dis 1972;25:473-479.
- TOWNSEND JL. Smoking and lung cancer: a cohort data study of men and women in England and Wales 1935-1970. J R Statist Soc A 1978;141:95-107.
- MANTON KG, STALLARD E. A population-based model of respiratory cancer incidence, progression, diagnosis, treatment, and mortality. Comput Biomed Res 1982;15:342-360.
- HORM JW, ASIRE AJ. Changes in lung cancer incidence and mortality rates among Americans: 1969-78. JNCI 1982;69:833-837.
- CUMMINGS KM. Changes in the smoking habits of adults in the United States and recent trends in lung cancer mortality. Cancer Detect Prev 1984;7:125-134.
- HAKULINEN T, PUKKALA E. Future incidence of lung cancer: forecasts based on hypothetical changes in the smoking habits of males. Int J Epidemiol 1981;10:233-240.
- JANERICH DT. Forecasting cancer trends to optimize control strategies. JNCI 1984;72:1317-1321.
- National Center for Health Statistics. Health, United States, 1984. Washington, DC: US Govt Print Off, 1984 (DHHS publication No. (PHS)84-1232).
- Office on Smoking and Health. Public Health Service, US Department of Health and Human Services. The health consequences of smoking. Cancer. A report of the Surgeon General. Washington, DC: US Govt Print Off, 1982 (DHHS publication No. (PHS)82-50179).
- TODD GF, LEE PN, WILSON MJ. Cohort analysis of cigarette smoking and of mortality from four associated diseases. London: Tobacco Research Council, 1976.
- KERMACK WO, MCKENDRICK AG, MCKINLAY PL. Death rates in Great Britain and Sweden: expression of specific mortality rates as products of two factors and some consequences thereof. J Hyg (Lond) 1934;34:433-457.
- BARRETT JC. The redundant factor method and bladder cancer mortality. J Epidemiol Community Health 1978;32:314-316.
- DAY NE, CHARNAY B. Time trends, cohort effects, and aging as influence on cancer incidence. In: Magnus K, ed. Trends in cancer incidence (causes and practical implications). Washington, DC: Hemisphere, 1982;51-65.
- STEVENS RG, MOOLGAVKAR SH. A cohort analysis of lung cancer and smoking in British males. Am J Epidemiol 1984;119:624-641.
- OSMOND C, GARDNER MJ. Age, period and cohort models applied to cancer mortality rates. Stat Med 1982;1:245-259.
- HOLFORD TR. The estimation of age, period and cohort effects for vital rates. Biometrics 1983;39:311-324.
- KUPPER LL, JANIS JM, KARMOUS A, et al. Statistical age-period-cohort analysis: a review and critique. J Chronic Dis 1985;38:811-830.
- MOOLGAVKAR SH. Risk assessment using vital data. In: Prentice RL, Whittemore AS, eds. Environmental epidemiology: risk assessment. Philadelphia: Society of Industrial and Applied Mathematics, 1982;175-192.
- RODGERS WL. Estimable functions of age, period, and cohort effects. Am Soc Rev 1982;47:774-787.
- US Federal Trade Commission. A report to Congress pursuant to the Federal Cigarette Labeling and Advertising Act for the year 1981. July, 1984.
- American Cancer Society. U.S. tar/nicotine levels dropping. World Smoking and Health 1981;6:47.
- PEACE LR. A time correlation between cigarette smoking and lung cancer. The Statistician 1985;34:371-381.
- PICKLE LW, CORREA P, FONTHAM E. Recent case-control studies of lung cancer in the United States. In: Mizell M, Correa P, eds. Lung cancer: causes and prevention. Deerfield Beach, FL: Verlag Chemie Int, 1984;101-115.
- GARFINKEL L. Time trends in lung cancer mortality among nonsmokers and a note on passive smoking. JNCI 1981;66:1061-1066.
- LEE PN. Lung cancer incidence and type of cigarette smoked. In: Mizell M, Correa P, eds. Lung cancer: causes and prevention. Deerfield Beach, FL: Verlag Chemie Int, 1984;273-283.
- LUBIN JH, BLOT WJ, BERRINO F, et al. Modifying risk of developing lung cancer by changing habits of cigarette smoking. Br Med J 1984;288:1953-1956.
- LUBIN JH, BLOT WJ, BERRINO F, et al. Patterns of lung cancer risk according to type of cigarette smoked. Int J Cancer 1984;33:569-576.
- NELDER JA, WEDDERBURN RWM. Generalized linear models. J R Statist Soc A 1972;135:370-384.
- Office of the Assistant Secretary for Health. Office on Smoking and Health. Public Health Service, US Department of Health and Human Services. The changing cigarette: a report of the Surgeon General. Washington, DC: US Govt Print Off, 1981 (DHHS publication No. (PHS)81-50156).
- GREENWALD P, SONDIK FI. Cancer control objectives for the nation: 1985-2000. NCI Monogr 1986;2:3-93.
- SHOPLAND DR, BROWN C. Area review: current trends in smoking control. Ann Behav Med 1985;7:5-8.

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